

TABLE 12. Clinically significant drug–drug interactions involving the rifamycins*

Drug class	Drugs whose concentrations are substantially decreased by rifamycins (references)	Comments
Anti-infectives	HIV-1 protease inhibitors (saquinavir, indinavir, nelfinavir, amprenavir, ritonavir, lopinavir/ritonavir) (1,20–25)	Can be used with rifabutin. Ritonavir, 400–600 mg twice daily, probably can be used with rifampin. The combination of saquinavir and ritonavir can also be used with rifampin.
	Nonnucleoside reverse transcriptase inhibitors Delavirdine (26,27) Nevirapine (28) Efavirenz (29)	Delavirdine should not be used with any rifamycin. Doses of nevirapine (28) and efavirenz (29) need to be increased if given with rifampin, no dose increase needed if given with rifabutin (5).
	Macrolide antibiotics (clarithromycin, erythromycin) (30–32)	Azithromycin has no significant interaction with rifamycins.
	Doxycycline (33)	May require use of a drug other than doxycycline.
	Azole antifungal agents (ketoconazole, itraconazole, voriconazole) (34–38)	Itraconazole, ketoconazole, and voriconazole concentrations may be subtherapeutic with any of the rifamycins. Fluconazole can be used with rifamycins, but the dose of fluconazole may have to be increased.
	Atovaquone (39)	Consider alternate form of <i>Pneumocystis carinii</i> treatment or prophylaxis.
	Chloramphenicol (40)	Consider an alternative antibiotic.
	Mefloquine (41)	Consider alternate form of malaria prophylaxis.
Hormone therapy	Ethinylestradiol, norethindrone (42–44)	Women of reproductive potential on oral contraceptives should be advised to add a barrier method of contraception when taking a rifamycin.
	Tamoxifen (45)	May require alternate therapy or use of a nonrifamycin-containing regimen.
	Levothyroxine (46,47)	Monitoring of serum TSH recommended; may require increased dose of levothyroxine.
Narcotics	Methadone (48,49)	Rifampin and rifapentine use may require methadone dose increase; rifabutin infrequently causes methadone withdrawal.
Anticoagulants	Warfarin (50)	Monitor prothrombin time; may require two- to threefold dose increase.
Immunosuppressive agents	Cyclosporine, tacrolimus (51–53)	Rifabutin may allow concomitant use of cyclosporine and a rifamycin; monitoring of cyclosporine serum concentrations may assist with dosing.
	Corticosteroids (54–57)	Monitor clinically; may require two- to threefold increase in corticosteroid dose (58).
Anticonvulsants	Phenytoin (59), lamotrigine (60)	Therapeutic drug monitoring recommended; may require anticonvulsant dose increase.
Cardiovascular agents	Verapamil (61), nifedipine (62,63), diltiazem (a similar interaction is also predicted for felodipine and nisoldipine)	Clinical monitoring recommended; may require change to an alternate cardiovascular agent.
	Propranolol (64), metoprolol (65)	Clinical monitoring recommended; may require dose increase or change to an alternate cardiovascular drug.
	Enalapril (66), losartan (67)	Monitor clinically; may require a dose increase or use of an alternate cardiovascular drug.
	Digoxin (among patients with renal insufficiency) (68), digitoxin (69)	Therapeutic drug monitoring recommended; may require digoxin or digitoxin dose increase.
	Quinidine (70,71)	Therapeutic drug monitoring recommended; may require quinidine dose increase.
	Mexilitine (72), tocainide (73), propafenone (15)	Clinical monitoring recommended; may require change to an alternate cardiovascular drug.
Bronchodilators	Theophylline (74)	Therapeutic drug monitoring recommended; may require theophylline dose increase.
Sulfonylurea hypoglycemics	Tolbutamide, chlorpropamide, glyburide, glimepiride, repaglinide (75–79)	Monitor blood glucose; may require dose increase or change to an alternate hypoglycemic drug.
Hypolipidemics	Simvastatin (80), fluvastatin (81)	Monitor hypolipidemic effect; may require use of an alternate hypolipidemic drug.
Psychotropic drugs	Nortriptyline (82)	Therapeutic drug monitoring recommended; may require dose increase or change to alternate psychotropic drug.
	Haloperidol (83), quetiapine (84)	Monitor clinically; may require a dose increase or use of an alternate psychotropic drug.
	Benzodiazepines (e.g., diazepam [85], triazolam [86]), zolpidem (87), buspirone (88)	Monitor clinically; may require a dose increase or use of an alternate psychotropic drug.

* For reference citations refer to Section 7.2.